E.s.r. Evidence for the Multiplicity of Side-chain Oxidation Pathways in the Acid-catalysed Decomposition of Substituted Hydroxycyclohexadienyl Radicals

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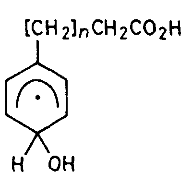
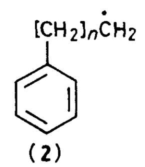
Addition of $^{\bullet}$OH to the aromatic rings of 3-phenylpropanoic acid and 3-phenylpropanol is followed at low pH by two competing processes, oxidation at the side-chain terminus and loss of a benzylic hydrogen atom, in both of which radical-cations are believed to mediate.

The hydroxyl radical attacks aromatic rings more readily than it abstracts hydrogen from C–H or O–H bonds,[1] yet under acidic conditions side-chain oxidation has also been observed.[2] With 3-phenylpropanoic acid, for example, e.s.r. signals from (**1**, $n = 1$) are replaced by those from (**2**, $n = 1$) as the pH is reduced below *ca.* 3.[2] The mechanism of reaction (decarboxylation in this example) is unclear and may be related to the mechanism of oxidation of related compounds by, for example, $SO_4^{\bullet -}$,[3] where 'remote' side-chain oxidation [*e.g.* the oxidative decarboxylation of 4-phenylbutanoic acid to give products from (**2**, $n = 2$)] can accompany the formation of products whose generation probably involves deprotonation of a first-formed radical-cation [*e.g.* (**3**, $n = 2$) from 4-phenylbutanoic acid].[4] Thallium(III) brings about similar transformations.[5]

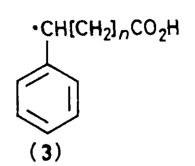
In the reaction of $Ph[CH_2]_2CO_2H$ with $^{\bullet}$OH (generated from Ti^{III} and H_2O_2 in a continuous flow system) we find that e.s.r. signals from (**1**, $n = 1$) and its isomers are steadily



(1)



(2)



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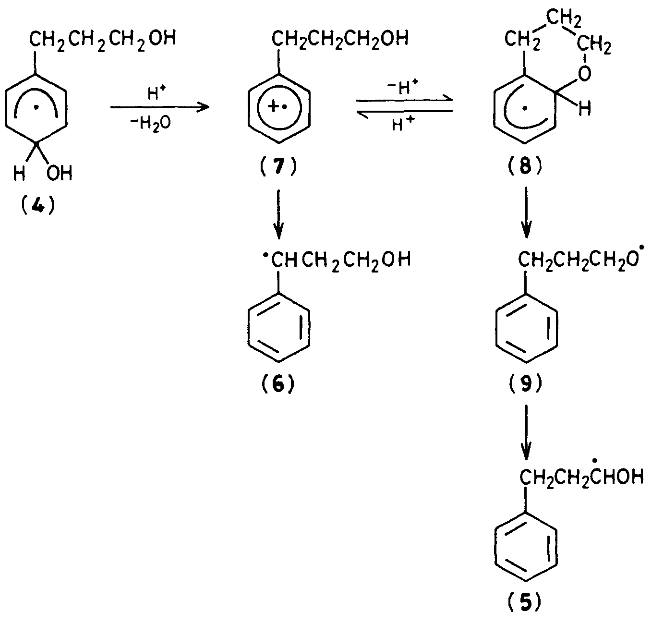
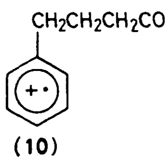


Scheme 1

replaced by that from (**2**, n = 1) as the pH is lowered below 3.5, and that this signal is in turn replaced by that from (**3**, n = 1) below pH *ca.* 1.8. $Ph[CH_2]_3CO_2H$ behaves similarly, giving (**1**, n = 2) above pH *ca.* 3.5, the radical (**2**, n = 2) in the region pH 3.5—1.5, and (**3**, n = 2) as the dominant radical below pH 2.5.† The former substrate also reacts with $SO_4^{\bullet-}$ (from Ti^{III} and $S_2O_8^{2-}$) to give the appropriate decarboxylated and benzylic radicals in the pH ranges >1.5 and <1.5, respectively.

Analogous behaviour is observed for the reaction between hydroxyl radicals and $Ph[CH_2]_3OH$: as the pH is lowered, signals from cyclohexadienyl radicals (**4**) are steadily replaced by the spectrum from (**5**) (below pH 3), which is succeeded by (**6**) (below pH 1.5). In contrast, $Ph[CH_2]_4CO_2H$, $Ph[CH_2]_4OH$, and $Ph[CH_2]_3OMe$ give hydroxycyclohexadienyl radicals and, below pH *ca.* 1.5, benzylic species; no species analogous to (**5**) are detected.

We believe that the results for 3-phenylpropanol imply the formation from a first-formed hydroxyl-adduct of an intermediate which can decompose to achieve effective remote side-chain oxidation yet also produce under more acidic conditions the precursor of (**6**) (see Scheme 1). The latter is believed to be the radical-cation (**7**) (species of this type are formed *directly* in reaction with $SO_4^{\bullet-}$). Our evidence suggests that the former intermediate is the cyclic radical (**8**), formed either *via* internal nucleophilic attack on (**7**) or directly from (**4**); the radical (**8**) can decompose to (**9**), which is known[6] to give (**5**) rapidly under these conditions. Thus the remote oxidation does not proceed effectively for a longer side-chain or when ring-formation is prevented by the incorporation of the oxygen in an ether function; further, direct electron-transfer from oxygen to the ring can probably be ruled out since such a process should occur more readily for the ether than the corresponding alcohol and in both cases should be unfavourable (*cf.* ionization potentials[7] for toluene, diethyl ether, and ethanol of 8.82, 9.53, and 10.48 eV, respectively). The isolation of 3,4-dihydro-2*H*-1-benzopyran from the reaction of $Ph[CH_2]_3OH$ (*cf.* also ref. 5) and the recent evidence[8] for acid-catalysed reactions analogous to the transformation (**8**) → (**7**) [and subsequently (**6**)] also provide support for our interpretation.



(10)

For the appropriate acids we believe that an essentially similar scheme is operating, though the decarboxylation pathway (presumably *via* $Ph[CH_2]_{n+1}CO_2^{\bullet}$) may involve *direct* electron-transfer rather than a discrete σ-bonded intermediate akin to (**8**). The pH changes observed may reflect the greater nucleophilicity of the carboxylate ion (**10**) compared with its protonated counterpart, or the expected ease of one-electron oxidation of the carboxylate in the former, compared with the latter, or both.

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† The spectral parameters of radicals detected are entirely consistent with previous analyses and assignments to cyclohexadienyl, alkyl, and benzyl radicals (see *e.g.* ref. 2); full details of the experimental results, including spectra, will be reported subsequently.